

Interleukin-6/ GP80-dependent pathways role in physiologic cachexia during liver regeneration after partial hepatectomy

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Liver has a unique capacity to regenerate its mass after tissue loss. Many of the cytokines and growth factors were shown to be critical in liver regeneration. Studies with interleukin-6 (IL-6) – deficient mice demonstrated that IL-6 plays central role in hepatocyte proliferation via activating signal transducer and activator of transcription 3 (STAT3). The biological activities of IL-6 are potentiated when it binds to an 80 kDa IL-6 (IL-6Ra) receptor located on target cells. IL-6 and IL-6Ra complex then associates with another glycoprotein, gp130, to initiate intracellular signaling.

Another of many IL-6 functions is metabolic control of the body. Increased activation of IL6 and STAT3 due to acute body injury, such as partial hepatectomy, causes metabolic dysregulation associated with sustained muscle and adipose tissue loss, a condition called physiologic Cachexia.

Two lines of transgenic mice with conditional knockout of gp 80 in the liver and conditional knockout of gp 80 in the muscle were generated to investigate the role of IL6 in liver regeneration and concomitant muscle wasting after partial hepatectomy. Here, we report that specific interruption of IL-6 pathway in the liver was presented with normal liver regeneration but associated with increased animal mortality after partial hepatectomy. Conversely, specific abrogation of IL-6 pathway in muscle lead to increased liver regeneration that did not increase muscle or adipose tissue wasting. These findings suggest that IL-6 pathway may play a central role in the liver regeneration and muscle wasting axis.